

**REMARKS**

Claims 1-10, 13, 15-18, and 23-38 have been withdrawn from consideration. Claims 11, 12, 14, and 19-22 have been rejected. Applicants respectfully note Claim 13 has been rejected in the present Office Action, as well as Claims 10-22. Applicants believe the Office Action meant Claim 14 and Claims 19-22.

Claim 11 has been rewritten to improve the readability of the claim. As such, the claim recites the composition is the reaction product of a flowable prepolymer (Prepolymer A) and a linear, star, dendrimeric, or hyperbranched soft segment forming functional oligomer (Component B) having degradable arms. Support for this amendment is found at page 18, ll. 11-15. Claim 11 has been further amended to replace the term “to form” with the term “thereby forming.”

Claim 12 has been amended to recite “said functional oligomer having degradable arms.” Support for this amendment can be found at page 18, ll. 14-17, the figures on pages 19-20, and at page 21, ll. 2-4. Claim 12 has been further amended to correct the typographical errors wherein the term “dendrimer” is amended to recite “dendrimeric” and a comma is inserted after the words “linear,” “star,” and “dendrimeric.” Claim 12 has also been amended to change the word “comprising” to “comprises” to improve the readability of the claim.

No new matter is believed to have been added by these amendments; therefore, examination is requested on the claims as amended herewith.

**REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH**

The Office Action has rejected Claims 11-12, 14, and 19-22 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants believe the present amendments to Claim 11 render this rejection moot. As such, Applicants respectfully request reconsideration and withdrawal of this rejection.

The Office Action has rejected Claim 22 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite because of the use of the term “sodium chloride type salts.” The skilled artisan would understand this term to mean the use of a salt as a porogen, i.e., a salt that can create pores during a post synthesis leaching process. This process is well known in the art.

Other salts, for example, potassium chloride would also be effective. "Sodium chloride type salts" are those that are highly water soluble. Applicants describe these porogens at page 22, ll. 1-11. As such, any water soluble, leachable material, for example, sodium chloride, potassium chloride, and sugar can be used to form the pores. Applicants respectfully request reconsideration and withdrawal of this rejection.

The Office Action further rejects Claim 11 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite because of the use of the term "to form." Applicants believe the amendment to Claim 11 overcomes this rejection. Applicants respectfully request reconsideration and withdrawal of this rejection.

**REJECTIONS UNDER 35 USC § 102(b)**

The Office Action has rejected Claims 11-12 and 19-22 under 35 U.S.C. § 102(b), as allegedly being anticipated by U.S. 4,412,033 (hereinafter "LaBelle"). Applicants respectfully disagree.

As a first issue, the Office Action states:

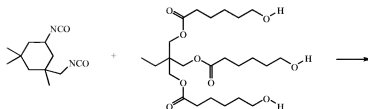
In the instant case, the same product is made whether the diisocyanate is first added to the poly(caprolactone) triol and subsequently treated with pentaerythritol (as done by [LaBelle]) or if the diisocyanate is first added to pentaerythritol and subsequently treated with the poly(caprolactone) triol (as presently claimed).

As such, the Office Action alleges that when forming a polymer composition (or any composition comprising a series of steps), for example, a process requiring steps as recited in Claim 11, that the order of addition is inconsequential as to what products are formed. Applicants strongly disagree. The order of addition of reagents is a critical feature that allows one final composition to be formed in favor of another.

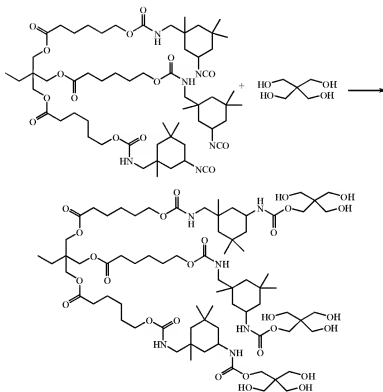
Applicants provide the following example to show the importance that the order of addition has in determining the final reaction product. The first example is depicted in Scheme I below. In Step (i), isophorone diisocyanate (IPDI) is reacted with poly(caprolactone) triol to form an IPDI capped poly(caprolactone) triol. In Step (ii) the IPDI capped poly(caprolactone) triol is further reacted with pentaerythritol to form the final composition (A).

Scheme I

Step (i)



Step (ii)

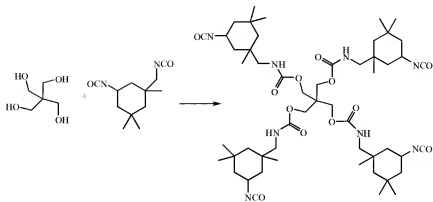


(A)

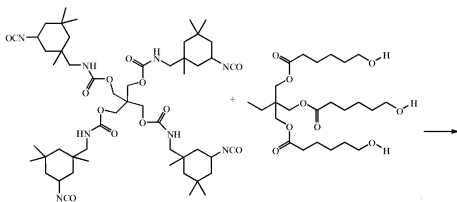
The second example, wherein the order of addition is reversed, is depicted in Scheme II below. In Step (i) isophorone diisocyanate (IPDI) is reacted with pentaerythritol to form an IPDI capped pentaerythritol. In Step (ii) the IPDI capped pentaerythritol is further reacted with poly(caprolactone) triol to form the final composition (B).

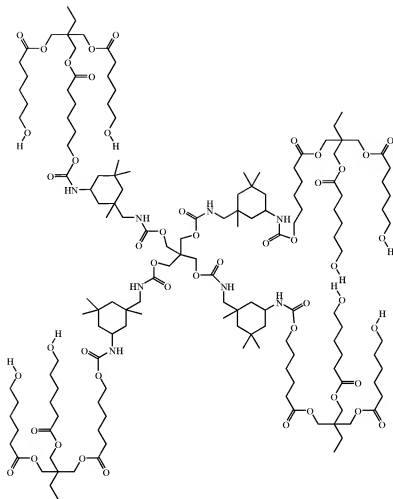
Scheme II

Step (i)



Step (ii)





(B)

When comparing the reaction products of Scheme I and II, it is clear the reaction products are different. For example, composition (A) comprises a pentaerythritol:isophorone diisocyanate: poly(caprolactone) triol ratio of 3:3:1 whereas composition (B) comprises a pentaerythritol: isophorone diisocyanate: poly(caprolactone) triol ratio of 1:4:4. Also, the molecular weight of (A) is approximately 1551 g/mol whereas the molecular weight of (B) is approximately 2931 g/mol; almost twice as high. In addition, composition (A) has 9 hydroxyl groups for crosslinking whereas composition (B) has only 8. As such, on a weight per weight basis composition (A) has twice the number of free hydroxyls. Applicants feel this example clearly shows that the order of addition does affect the final product and, contrary to the Office Action's allegations, the same product is **not** made when the order of reagents is reversed.

The order of addition, as recited in Claim 11, is important because the biodegradable biocompatible polyurethane/urea polymer compositions recited therein have palpably different properties than those disclosed in LaBelle. Attached herewith is a Declaration under 37 C.F.R. § 1.132 by Dr. Pathiraja Gunatillake that describes the clear differences between the composition of Claim 11 and those of LaBelle. A copy of Dr. Gunatillake's *Curriculum Vitae* is attached herewith as Appendix A.

For example:

1. LaBelle discloses at col. 3, ll. 42-44 "[t]he prepolymer composition is curable at temperatures above 60 °C. (preferably above 85 °C)." As explained by Dr. Gunatillake, this initial curing temperature when taken together with the enthalpy of formation of the crosslinking reaction would raise the temperature of LaBelle's composition to 103 °C during curing. And this is not even the preferred range above 85 °C which would raise the temperature to at least 128 °C. By contrast, Applicants disclose polymers curable at room temperature.
2. LaBelle discloses compositions that are useful as adhesives, coating, sealants, and the like. Adhesives, coatings, sealants, etc. would not function properly if they were biodegradable. Applicant's compositions are biodegradable.
3. LaBelle's disclosed compositions are not biocompatible. For example, LaBelle's only example of a composition comprises the plasticizer HB-40. As stated by Dr. Gunatillake, this plasticizer is toxic and would not be used for compositions applied to tissue.

When poly(caprolactone) triol and a diisocyanate are reacted together in a first step according to the conditions disclosed by LaBelle, the products formed are not the products obtained by the order of addition recited in the present claims. For example, this reaction step as taught by LaBelle results in a mixture that comprises unreacted diisocyanate, a plurality of different species of isocyanate capped poly(caprolactone), *inter alia*, mono-, di- and tri-capped species, as well as a species that is the reaction product of two or more molecules of poly(caprolactone) triol linked by a diisocyanate. By contrast, Claim 11 recites a process wherein pentaerythritol, for example, is first reacted with a diisocyanate. As such, different species of isocyanate capped pentaerythritol, including mono-, di-, tri- and tetra-capped species,

as well as multiple molecules of pentaerythritol linked by diisocyanates. Dr. Gunatillake in his Declaration addresses this difference between the process disclosed by LaBelle and that recited in Claim 11 and provides a GPC trace (Exhibit 5) of the reaction products formed by the process disclosed by LaBelle. As explained by Dr. Gunatillake the complex reactions and side reactions that can occur under the conditions disclosed by LaBelle will result in a composition not recited in the present claims.

LaBelle clearly defines and characterizes his compositions; high temperature necessary for curing, different order of addition resulting in compositions having different properties, as well as different intended end usage. LaBelle's compositions do not anticipate Applicants' compositions as recited in Claim 11. Applicants respectfully request reconsideration and withdrawal of the rejection of the Claims over LaBelle.

The Office Action has rejected Claims 11 and 19-22 under 35 U.S.C. § 102(b), as allegedly being anticipated by U.S. 4,293,679 (hereinafter "Cogliano"). Applicants respectfully disagree.

The Examiner states that Cogliano "discloses a polyurethane prepolymer (a flowable prepolymer) prepared by the reaction product of a polyol, such as, pentaerythritol...and a diisocyanate (see abstract; col. 5, lines 7-31). A third polyol, such as sucrose (a hyperbranched soft segment forming functional oligomer with degradable arms) may be added to the reaction...Based on the substantially identical process using identical components, the Examiner has a reasonable basis to believe that the properties claimed in the present invention are inherent in the composition of [Cogliano]."

As addressed in his Declaration, Dr. Gunatillake points out that Cogliano discloses the reaction of a polyoxyethylene glycol (PEG) with a molar excess of diisocyanate to form an isocyanate capped polyurethane product (A) (column 5, lines 7-12). Separately, a polyol, i.e., pentaerythritol, is reacted with a large molar excess of diisocyanate to form an isocyanate capped polyurethane intermediate product (B). These two products are then blended and subsequently crosslinked (column 5, lines 16-26). The crosslinking is affected by a large excess of water. Curing the composition in the presence of water results in a polymer that is largely amine terminated rather than urethane linked. Much of the isocyanate will undergo reaction with water

to form amine groups. A summary of Cogliano's reaction sequence is depicted in Exhibit 4 of Dr. Gunatillake's Declaration.

Furthermore, Claim 11 (as amended) recites the reaction product of a multifunctional core molecule having a molecular weight less than or equal to 400 and an isocyanate that is subsequently reacted with a functional oligomer having degradable arms, for example, the functional oligomers as recited in Claim 12. This composition is distinguished from the disclosure of Cogliano because only one component (i.e., the low molecular weight multifunctional core molecule) is reacted with isocyanate prior to adding the functional oligomer having degradable arms, whereas Cogliano discloses that **both** components are reacted with excess isocyanate prior to combining. Accordingly, as pointed out by Dr. Gunatillake the final product formed in each case will be different. The skilled artisan would understand that combining two materials (as disclosed by Cogliano) having no free hydroxyl groups (**all** of Cogliano's hydroxyls have been converted to isocyanate) would yield very different compositions than combining two materials wherein only one has been functionalized with isocyanate, the other having many free hydroxyls still present. See Cogliano at col. 5, ll. 7-31.

The compositions obtained by the process disclosed by Cogliano do not result in the same compositions that Applicants process provides, nor would the artisan expect the final properties of Cogliano's compositions to be the same. Applicants respectfully request reconsideration and withdrawal of the rejection of the Claims over Cogliano.

#### **REJECTIONS UNDER 35 USC § 103(a)**

The Office Action has rejected Claims 11-12, 14, and 19-22 under 35 U.S.C. § 103(a), as allegedly being obvious over LaBelle in view of U.S. 4,908,406 (hereinafter "Mulhaupt"). Applicants respectfully disagree.

The Office Action states "[LaBelle] fails to disclose incorporation of methyl 2,6-diisocyanato hexanoate as the isocyanate" and that "[Mulhaupt] teaches that methyl 2,6-diisocyanato hexanoate is known in the art as a compound which links a polyol and a polyhydroxy compound providing a cured polyurethane adhesive (see col. 1, ll. 4-7; col. 2, lines 50-59)." Moreover, the Office Action further states "[LaBelle] and [Mulhaupt] are both directed to preparing cured polyurethane adhesives. The rationale to incorporate methyl 2,6-diisocyanato



hexanoate into the formulation of [LaBelle] is (1) the compound is known to serve as a linker between polyols and polyhydroxy compound to provide cured polyurethane adhesives and (2) it meets the structural and functional requirements taught by [LaBelle], namely that it is aliphatic and has functionality greater than 1 but less than 4.”

The mere fact that a compound, i.e., methyl 2,6-diisocyanato hexanoate, can function as a crosslinking agent does not mean that incorporation of this crosslinking agent into the disclosure of LaBelle will result in the same compositions as obtained by the order of addition recited in Claim 11. LaBelle **does not teach that the order of addition is consequential** to the compositions formed by his process. Indeed, as discussed herein above, the compositions that result from the process disclosed by LaBelle are not the same compositions as obtained by Claim 11’s order of addition. Therefore, incorporation into LaBelle of any reagent without the teaching that the order of addition is critical, does not make the process of LaBelle capable of providing the same compositions that are formed by the process recited in Claim 11.

The polyurethane systems disclosed by LaBelle are adhesives, coatings, sealants, and the like. By contrast the compositions recited in the present claims are useful for biomedical applications and, as such, must be biodegradable. All of LaBelle’s examples comprise a plasticizer, for example, HB-40, which is a high boiling hydrogenated aromatic. This type of plasticizer would be necessary to formulate the higher molecular weight polyurethanes of LaBelle. Moreover, these necessary plasticizers are unsuitable for bio-medical applications.

As it relates to the issue of obviousness, a failure to recognize details of a prior art disclosure can lead to an improper conclusion regarding the differences between the claimed invention and the prior art. An example of this failure to recognize differences was a key issue before the Federal Circuit in *Süd-Chemie, Inc. v. Multisorb technologies, Inc.* (2008-1247) decided January 30, 2009.

In its obviousness analysis, the lower court had determined that a prior art reference disclosed the claimed container except for the inclusion of an absorbent substance that is encapsulated by the packaging materials. The claims at issue require a laminate film comprised of “compatible” polymeric materials. The lower court concluded that the prior art reference taught such materials because “it suggests employment of the same materials claimed by the [patent-in-suit] to be ‘compatible polymeric materials’.”

On appeal, Süd-Chemie successfully argued that the lower court had only matched the classes of materials - polyethylenes, polypropylenes, and polyolefins - mentioned by the two patents and had failed to recognize that these classes have large numbers of substances with widely varying properties. The Federal Circuit found this argument persuasive, noting that the prior art patent only disclosed the use of incompatible materials. Since the claims at issue require the use of compatible polymeric materials, this difference between the claims must be addressed in the obviousness inquiry. The Court ruled:

It is therefore evident that even though the patents disclose the same classes of polymeric materials used to form the packaging material, the containers described in Komatsu and in the '942 patent are different in a way that the '942 patent treats as important to the invention....The district court looked only to the classes of materials described in the patents and did not examine the softening points of the materials. It therefore failed to recognize that Komatsu discloses the use of incompatible materials where the '942 patent requires compatible materials, and it therefore incorrectly concluded that Komatsu teaches the same container as that claimed in the '942 patent. (Emphasis added.)

For the process recited in Claim 11, the order of addition is “important to the invention.” This order of addition allows the formation of compositions having “important properties critical to the invention.” Applicants disclose at page 21, ll. 14- 19:

The mechanical properties of cured scaffolds according to the invention are highly desirable. In particular, the cured scaffolds of the invention have good compressive strength. Figure 1 shows the effect of water lactose and triethylene glycol on compressive strength of cured polymer compositions of the invention. They can also be sterilized using, for example, gamma radiation, and will degrade in appropriate time frames by oxidative or hydrolytic degradation. (Emphasis added.)

Applicants further disclose at page 6, ll. 23-26:

It is surprisingly found that the prepolymer compositions according to the invention have a viscosity which enables them to be utilized in a

flowable form, and combined with a cross linker for delayed or slow curing thus making them especially suited to biological application including tissue engineering and repair.

In addition, Applicants disclose compositions “having a compressive strength in the range of 0.05–80 MPa” (Claim 20) and “having pores in a size range of 150-300 micron” (Claim 21). Moreover, the Office Action particularly recognizes that LaBelle does not adequately disclose what is important to Applicants’ process when stating at page 5 “[LaBelle] does not appreciate that the composition has compressive strength in the range of 0.05-80 MPa nor that the product has pores in a size range of 150-300 microns.” Applicants’ compositions are useful in biological applications, whereas LaBelle discloses (col. 14, ll. 30-31) compositions useful as adhesives for “bond[ing] acid-etched aluminum to itself and aluminum to sheet-molding compound (SMC).”

The mere fact that Mulhaupt discloses “methyl 2,6-diisocyanato hexanoate...as a compound which links a polyol and a polyhydroxy compound” does not provide the artisan with any more reason to consider LaBelle as a reference which teaches or suggests Applicants’ order of addition, and, hence, Applicant’s compositions. As such, LaBelle, even in view of Mulhaupt, only teaches a process for making compositions that are formed under conditions not recited in Applicants’ claims or that have properties taught Applicants. Therefore, contrary to the Court’s decision in *Süd-Chemie*, the Office Action has not established that LaBelle in view of Mulhaupt treats as important to the Applicants’ process the order of addition as recited in Claim 11. Applicants therefore respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) of the Claims over LaBelle in view of Mulhaupt.

### **CONCLUSION**

In light of the foregoing amendments and remarks, it is believed that the rejections presented in the Final Office Action have been overcome. Accordingly, Applicants respectfully submit that the Application is allowable and seek notification of same. Further, in light of the allowance of the presently examined claims, Applicants seek rejoinder of at least withdrawn claims 13, 15-18, 23-25, 29, 30, and 33-38.

A credit card payment submitted *via* EFS Web in the amount of \$1,110.00, representing the fee for a Three-month extension of time (large entity) under 37 C.F.R. § 1.17(a)(3) is enclosed. This amount is believed to be correct; however, the Commissioner is hereby

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**APPLICATION NO. 10/520,414**

authorized to charge any additional fees which may be required, or credit any overpayment to  
Deposit Account No. 14-0629.

Respectfully submitted,

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